**RINGKASAN HASIL EVALUASI**
**PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK**
**VAKSIN HEPATITIS B FASE 3**
**PRODUKSI PT. BIOFARMA**

**Informasi Umum**

1. Hepatitis B dengan bahan aktif HBsAg impor dari *The Jannsen Vaccine Corp* telah terdaftar di Indonesia dengan produsen dan pendaftar PT. Bio Farma, Tbk. (GKL9802905543A1). Untuk memenuhi suplai vaksin program imunisasi nasional dan kemandirian ketersediaan vaksin, PT. Bio Farma mengembangkan bulk hepatitis B yang diproduksi sendiri (*in-house production*) dan mengajukan uji klinik melalui jalur penilaian Obat Pengembangan Baru (OPB).
2. Pengajuan uji klinik Vaksin Hepatitis B fase 3 didukung oleh uji nonklinik dan uji klinik fase1.

**Informasi Uji Klinik**

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| 1. | Judul Protokol | : | *Immunogenicity and Safety Following In-House Recombinant Hepatitis B (Bio Farma) vaccine compared to Hepatitis B (Bio Farma)® vaccine in Indonesian Population* (versi 1.b, 10 Agustus 2022) |
| 2. | Produk Uji | : | Recombinant Hepatitis B (registered vaccine) (HbsAg 20 mcg) diberikan 1 kali secara intramuskular<br>Produsen PT. Bio Farma |
| 3. | Produk Pembanding | : | Recombinant Hepatitis B (inhouse) (HbsAg 20 mcg) diberikan 1 kali secara intramuskular<br>Produsen PT. Bio Farma |
| 4. | Center / Peneliti | : | Departemen Ilmu Kesehatan Anak Fakultas Kedokteran Universitas Udayana, RS Sanglah, Bali / Dr. dr. I Gusti Ayu Trisna Windiani, SpA(K).<br>*Recruitment site:* Puskesmas 1 Denpasar Selatan, SD No 2 Sesetan, SMAN 5 Denpasar dan SMPN 6 Denpasar |
| 5. | Sponsor / ORK | : | PT. Bio Farma |
| 6. | Persetujuan Etik | : | No. No. 2738/UN14.2.2.VII.14/LT/2022 tanggal 30 Agustus 2022 dari Komite Etik Penelitian Fakultas Kedokteran Universitas Udayana |
| 7. | Desain Uji Klinik | : | *Experimental, randomized, double blind, four arm parallel group study, lot to lot consistency* |
| 8. | Jumlah Subjek | : | *540 subjects (10-40 years old)* |
| 9. | Tujuan Uji Klinik | : | *Primary Objective*<br>*T To assess the protectivity of In-House Recombinant Hepatitis B vaccine 28 days after 3 doses immunization.*<br><br>*Secondary Objective*<br>- *To describe immunogenicity of In-House Recombinant Hepatitis B vaccine.*<br>- *To assess the safety of In-House Recombinant Hepatitis B vaccine.*<br>- *To evaluate immunogenicity and safety in three consecutive batches of In-House Recombinant Hepatitis B vaccine.*<br>- *To evaluate immunogenicity and safety after primary series of investigational product compare to control.* |

10. Kriteria Eligibilitas : Kriteria Inklusi / *Inclusion criteria*

1. *Healthy individu as determined by clinical judgment, including a medical history and physical exam which confirms the absence of a current or past disease state considered significant by the investigator.*
2. *Subjects/parents/guardian(s) have been informed properly regarding the study and signed the informed consent form/ informed assent form.*
3. *Subject/parents/guardian(s) will commit to comply with the instructions of the investigator and the schedule of the trial.*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subject concomitantly enrolled or scheduled to be enrolled in another trial.*
2. *Subjects with known history of Hepatitis B contained vaccination in the last 10 years.*
3. *Evolving severe illness and/or chronic disease and fever (axillary temperature ³ 37.5°C) within the 48 hours preceding enrollment.*
4. *Known history of allergy to any component of the vaccines (based on anamnesis).*
5. *HBsAg positive.*
6. *Known history of immunodeficiency disorder (HIV infection, leukemia, lymphoma, or malignancy).*
7. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*
8. *Subject who has received in the previous 4 weeks a treatment likely to alter the immune response (intravenous immunoglobulins, blood-derived products or corticosteroid therapy and other immunosuppresant.*
9. *Pregnancy & Lactation (Adult).*
10. *Subject already immunized with any vaccine within 4 weeks prior and expects to receive other vaccines within 4 weeks following immunization.*

11. Luaran Uji Klinik/*Endpoint* : **Luaran Primer /** *Primary Endpoints*:

*The main evaluation criteria is number and percentage of subjects with anti HBsAg > 10mIU/ml, 28 days after the primary series of Hepatitis B vaccination for each group.*

**Luaran** Sekunder **/** *Secondary endpoints*

***Immunogenicity***

- *Serological response to the Hepatitis B vaccine recombinant: Geometric mean of anti-HBsAg, percentage of subjects with increasing antibody titer ≥ 4 times and/ or percentage of subjects with transition of seronegative to seropositive.*
- *Comparison of GMT, seroprotection, percentage of subjects with increasing antibody titer ≥4 times and/ or percentage of subjects with transition of seronegative to seropositive following primary series of investigational product compare to control.*

- *Comparison of GMT, seroprotection, percentage of subjects with increasing antibody titer ≥ 4 times and/ or percentage of subjects with transition of seronegative to seropositive following primary series between each number of investigational product.*

***Safety***

- *Immediate reaction within the first 30 minutes after each injection.*
- *Local and systemic events occurring after 30 minutes to 7 days after each injection.*
- *Local and systemic events occurring after 7 days to 28 days following injection.*
- *Any serious adverse event occurring from inclusion until 28 days after the last injection.*
- *Comparison of adverse events between investigational product (IP) and control.*
- *Comparison of adverse events between each batch number of IP.*

**Ringkasan Hasil Evaluasi**

Badan POM telah melakukan evaluasi protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 1 April 2022 dengan hasil sebagai berikut:

1. Berdasarkan hasil uji klinik fase I, Vaksin Rekombinan Hepatitis B produksi Bio Farma aman dan memberikan respon imun yang baik pada dewasa dan anak. Keamanan vaksin Rekombinan Hepatitis B produksi Bio Farma similar dengan Vaksin Hepatitis B yang telah teregistrasi. Imunogenisitas vaksin Rekombinan Hepatitis B produksi Bio Farma lebih tinggi dibandingkan Vaksin Hepatitis B yang telah teregistrasi
2. Desain uji klinik yang diajukan dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

**Keputusan**

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik (PPUK) No. RG.01.06.1.3.11.22.248 tanggal 15 November 2022.